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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Application Number: 10/501,236
Filing Date: July 12, 2004
Appellant(s): BECKERT ET AL.

Teddy S. Gron
Reg. No. 63,062
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 18 February 2010 appealing from the Office action mailed 19 August 2009.

(1) Real Party in Interest

The examiner has no comment on the statement, or lack of statement, identifying by name the real party in interest in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The following is a list of claims that are rejected and pending in the application:

Claims 1-8, 10-12 and 17 are pending.

Claims 1, 2, 4-8 and 10-12 are rejected.

Claim 17 stands withdrawn (non-elected invention).

Claims 9 and 13-16 are cancelled.

Claim 3 (previously rejected) is now deemed allowable.

(4) Status of Amendments After Final

The examiner has no comment on the appellant's statement of the status of amendments after final rejection contained in the brief.

(5) Summary of Claimed Subject Matter

The examiner has no comment on the summary of claimed subject matter contained in the brief.

(6) Grounds of Rejection to be Reviewed on Appeal

The examiner has no comment on the appellant's statement of the grounds of rejection to be reviewed on appeal. Every ground of rejection set forth in the Office action from which the appeal is taken (as modified by any advisory actions) is being maintained by the examiner except for the grounds of rejection (if any) listed under the subheading "WITHDRAWN REJECTIONS." New grounds of rejection (if any) are provided under the subheading "NEW GROUNDS OF REJECTION."

WITHDRAWN REJECTIONS

The following grounds of rejection are not presented for review on appeal because they have been withdrawn by the examiner.

With respect to Claim 3 ONLY, the 35 U.S.C. §103(a) rejection over Beckert (U.S. Pat. No. 6,632,454) has been withdrawn. Thus, claims 1, 2, 4-8 and 10-12 are rejected. Claim 3 is allowable.

(7) Claims Appendix

The examiner has no comment on the copy of the appealed claims contained in the Appendix to the appellant's brief.

(8) Evidence Relied Upon

6,632,454	BECKERT et al	10-2003

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

Claims 1, 2, 4-8 and 10-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Beckert *et al.* (hereinafter "Beckert") (WO 01/68058) (U.S. equivalent Pat. No. 6,632,454).

Beckert ('058) teaches a multilayer pharmaceutical product that substantially comprises a) a core containing a pharmaceutically active substance, b) an inner coating consisting of a copolymer or a mixture of copolymers that are composed of 85 to 98 wt.% of radically polymerized C_1 to C_4 alkyl esters of the acrylic or methacrylic acid and 15 to 2 wt.% of meth(acrylate) monomers with a quaternary ammonium group in the alkyl group, and c) an outer coating consisting of a copolymer that is composed of 75 to 95 wt.% of radically polymerized C_1 to C_4 alkyl esters of the acrylic or methacrylic acid and 5 to 25 wt.% of meth(acrylate) monomers with an anionic group in the alkyl group. The product is used for producing a pharmaceutical product that releases the active substance contained therein according to the USP release test, at pH 1.2 during 2 hours and subsequent rebuffering to pH 7.0, by less than 5% after 2.0 hours after start of the test and by 30 to 80% % after eight hours after start of the test (Abstract). The active substance can be budesonide. The dosage form includes a binder such as collidon 25 as well as an internal coat of Eudragit RS and RL and an external enteric coating of Eudragit FS (Example 1 - pages 16-18).

The instant invention would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, given the teachings of Beckert.

(10) Response to Argument

Appellant argues, "Beckert does not recognize the solubility and release problems associated with budesonide in the intestines. In fact, budesonide is but one of many active ingredients which Beckert '454 suggests for use as an active ingredient in its multilayer pharmaceutical products."

Appellant's arguments have been considered but were not deemed persuasive. In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies (*i.e.*, stability and/or low solubility problems encountered with budesonide) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Moreover, the reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve a different problem. It is not necessary that the prior art suggest the combination to achieve the same advantage or result discovered by applicant. See, e.g., In re Kahn, 441 F.3d 977, 987, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006). Note in particular that suitable drugs employed by Beckert include those having "adequate stability" such as "budesonide" (see col. 3, lines 50-59 of '454). Thus, the reference is clearly suggestive of the same objective (i.e., overcoming problems encountered with stability) as that sought herein by Appellant.

Appellant argues, "Beckert makes no distinction between 5-aminosalicylic acid and budesonide as the active ingredient".

This argument was not rendered persuasive. Beckert vividly suggests and teaches that corticosteroids, such as budesonide are suitable for use in their formulation. Thus, the listing and disclosure of budesonide as one of the possible active ingredients is a sufficient and positive teaching that cannot be ignored in the art and is ample to meet Appellant's requirement of the specific drug (budesonide) being claimed.

Appellant argues, "Beckert does not suggest making and using a pharmaceutical formulation which releases the budesonide content in an inner layer or core to the extent of more than 80% after 30 minutes in the intestines. The multilayer product in Beckert is designed to 'release less than 5% of the active pharmaceutical ingredient during the first 2 hours and from 30 to 80% of the active pharmaceutical ingredient 8 hours after the start of the test' (Beckert '454, Claim 1). Figure 1 of Beckert shows an active ingredient release from uncoated pellets with 5-aminosalicylic acid and Kollidon® 25 as the binder with release to an extent of less than 80% after 1 hour and 40% or less after 30 minutes. The evidence of record establishes that Kollidon® 25 binder employed in Beckert is a polyvinylpyrrolidone (PVP) which is neutral and does not contain acidic groups."

These arguments were not found convincing. While Beckert does not teach the instant rate of release of budesonide of more than 80% after 30 minutes, it is the position of the Examiner that the determination of effective or suitable release rates would be within the level of one of ordinary skill in the art, obtained via routine or manipulative experimentation to obtain optimal results, as these are variable parameters attainable within the art. With respect to Appellant's argument that "Kollidon® 25 is not an anionic polymer but a polyvinylpyrrolidone polymer which is neutral and therefore not a polymer or copolymer with acidic groups", it is

agreed that Kollidon® 25 is a polyvinylpyrrolidone polymer (and not an anionic polymer). However the teachings of the prior art are not limited to the examples disclosed therein and thus are not limited to the Kollidon® 25 binder employed in the examples. The reference as a whole must be taken into consideration. In this regard, note in particular that Beckert explicitly teaches a polymer or copolymer with acidic groups. Beckert teaches a multilayer pharmaceutical product that substantially comprises a) a core containing a pharmaceutically active substance, b) an inner coating consisting of a copolymer or a mixture of copolymers that are composed of 85 to 98 wt.% of radically polymerized C_1 to C_4 alkyl esters of the acrylic or methacrylic acid and 15 to 2 wt.% of meth(acrylate) monomers with a quaternary ammonium group in the alkyl group, and c) an outer coating consisting of a copolymer that is composed of 75 to 95 wt.% of radically polymerized C_1 to C_4 alkyl esters of the acrylic or methacrylic acid and 5 to 25 wt.% of meth(acrylate) monomers with an anionic group in the alkyl group. The dosage form includes a binder such as Kollidon® 25 as well as an internal coat of Eudragit® RS and RL and an external enteric coating of Eudragit® FS (see for instance, Example 1 beginning at column 7). Hence, Beckert clearly teaches a polymer or copolymer with acidic groups and is not limited to the use of Kollidon® 25. Thus, Beckert meets Appellant's claimed requirement for a "binder that is a polymer or copolymer with acidic groups" as recited in instant claim 1. In addition, based on these teachings of the prior art, Beckert also meets the recitations of instant claims 2, 4-6 and 12 which recite the desired binder of choice. Consequently, the prior art is well aware of combining a binder component as claimed with the particular active agent (budesonide) and is well aware of providing a structured formulation as is presently claimed herein.

Appellant argues, "Applicant's Specification acknowledged that there are solubility problems associated with using budesonide as the active ingredient in multi-layer formulations (Spec. p. 2, lines 33-37, p. 16, lines 10-17). Beckert does not recognize that budesonide has unique solubility problems."

This argument was not deemed persuasive. The argument that the prior art does not necessarily recognize the particular problem(s) to be treated does not negate the fact that the Beckert reference teaches a formulation as presently claimed and utilizes the same active component (budesonide) as employed by Appellant. As delineated above, the reason or motivation to modify the reference may often suggest what the inventor has done, but for a different purpose or to solve a different problem. It is not necessary that the prior art suggest the combination to achieve the same advantage or result discovered by applicant. See, e.g., *In re Kahn.* It is not incumbent that the prior art recognize the particular problem to be solved, in order to establish a *prima facie* case of obviousness. Where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a prima facie case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). In this instance, the art expressly teaches the same active agent - budesonide, employed in a multi-layered formulation and thus, based on the use of the same drug, it would be expected that the same problems (*i.e.*, solubility) would be encountered therein, absent a showing of evidence to the contrary.

Appellant argues, "The Examiner appear to agree with Applicant that Kollidon® 25 is a polyvinylpyrrolidone (PVP) and appears to agree that Kollidon® 25 is not a polymer with acidic groups. Thus, the Examiner appears to agree with Applicant that no core binder described in Beckert is a 'polymer or copolymer with acidic groups', which all of Appellant's claims require. (Appellant cites the BASF Technical Information Brochure dated January 2004, entitled "Soluble Kollidon® grades").

This argument was not persuasive. As discussed above, Beckert explicitly teaches a polymer or copolymer with acidic groups. Beckert teaches a multilayer pharmaceutical product that includes, among other components, an inner coating consisting of a copolymer or a mixture of copolymers that are composed of 85 to 98 wt.% of radically polymerized C_1 to C_4 alkyl esters of the acrylic or methacrylic acid and 15 to 2 wt.% of meth(acrylate) monomers with a quaternary ammonium group in the alkyl group, and c) an outer coating consisting of a copolymer that is composed of 75 to 95 wt.% of radically polymerized C_1 to C_4 alkyl esters of the acrylic or methacrylic acid and 5 to 25 wt.% of meth(acrylate) monomers with an anionic group in the alkyl group. The dosage form includes a binder such as Kollidon® 25 as well as an internal coat of Eudragit® RS and RL and an external enteric coating of Eudragit® FS (see for instance, Example 1 beginning at column 7). Hence, Beckert clearly teaches a polymer or copolymer with acidic groups and is not limited to the use of Kollidon® 25.

Appellant argues, "The evidence in the Specification (Examples 2-3 on pages 28-30) confirms that the release rates for budesonide bound in a binder which is a polymer or copolymer with acidic groups as per Applicant's claimed pharmaceutical formulation is significantly improved over the release rates shown and/or suggested by Beckert and are entirely unexpected."

This argument was not persuasive, as the determination of effective rates of release or profiles is within the level of the skilled artisan, obtained via a routine optimization process. The Beckert reference suggests and teaches use of a polymer or copolymer with acidic groups, as presently claimed herein.

Instant claims 3, 4 and 11 were argued separately and are discussed below:

Regarding claim 3, Appellant argues, "The Examiner has not explained why dependent claim 3 wherein the polymeric binder which binds budesonide in the inner layer of the claimed pharmaceutical formulation is a vinylpyrrolidone/vinyl acetate would have been prima facie obvious in view of Beckert's disclosure of Kollidon®25 PVP binder."

This argument was found persuasive, as Beckert does not disclose the selective binder of instant claim 3. Accordingly, the §103(a) rejection with respect to claim 3 only over Beckert has been withdrawn.

Regarding claim 4, Appellant argues, "The Examiner has not explained why dependent claim 4 would have been prima facie obvious in view of Beckert's disclosure of an intermediate layer comprising a meth(acrylate) copolymer which comprises 85 to 98% by weight free-radical polymerized C_1 to C_4 alkyl esters of the acrylic or methacrylic acid and 15 to 2 wt.% of meth(acrylate) monomers with a quaternary ammonium group in the alkyl group. Cationic quaternary ammonium groups are not anionic acidic groups. Beckert does not teach or suggest that its inner layer, i.e., intermediate layer of Applicant's claimed pharmaceutical formulation, should or may be a polymer or copolymer with acidic groups or a polymer or (meth)acrylate copolymer free of quaternary ammonium groups."

This argument was not found persuasive. Beckert discloses that their inner layer includes a polymer or copolymer with acidic groups. The Beckert inner coating (i.e., Appellant's intermediate layer) consists of a copolymer or a mixture of copolymers that are composed of 85 to 98 wt.% of radically polymerized C_1 to C_4 alkyl esters of the acrylic or methacrylic acid in addition to the 15 to 2 wt.% of meth(acrylate) monomers with a quaternary ammonium group in the alkyl group. Thus, the inclusion of polymers/copolymers with acidic groups is present in the inner coating of Beckert. Appellant's argument that "Beckert does not teach or suggest that its inner layer have a polymer or (meth)acrylate copolymer that is *free of* quaternary ammonium groups" was not persuasive since the instant claim language does not exclude the meth(acrylate) monomers with quaternary ammonium groups disclosed by Beckert. Quite to the contrary, the instant claims permit the inclusion of these polymers ((meth(acrylate) monomers with quaternary ammonium groups)) taught by Beckert based on the open-ended "comprising" claim language. The transitional term "comprising", which is synonymous with "including," "containing," or "characterized by," is inclusive or open-ended and does not exclude additional, unrecited elements or method steps. See, e.g., > Mars Inc. v. H.J. Heinz Co., 377 F.3d 1369, 1376, 71 USPQ2d 1837, 1843 (Fed. Cir. 2004) ("like the term comprising,' the terms containing' and mixture' are open-ended.").< Invitrogen Corp. v. Biocrest Mfg., L.P., 327 F.3d 1364, 1368, 66 USPQ2d 1631, 1634 (Fed. Cir. 2003). Thus, Appellant's arguments regarding claim 4 were not held persuasive.

Regarding claim 11, Appellant argues, "The Examiner has not explained why persons having ordinary skill in the art would employ two different kinds of the pharmaceutical formulations Beckert discloses in a multiparticulate pharmaceutical form with substantially

uniform release of budesonide in the small and large intestine, where one type of formulation releases the active ingredient predominantly in the pH range of the small intestine and the other type of formulation releases the active ingredient predominantly in the pH range of the large intestine. Beckert does not recognize that the release of the active ingredient may differ dependent on the environment in the small or large intestine."

This argument was not deemed persuasive. The Beckert reference is vividly suggestive of multiparticulate pellets or tablets compressed from pellets or pellets packed into capsules (see Claim 8 of Beckert) containing active agents such as budesonide. The Examples demonstrate testing of active ingredient release in a phosphate buffer at a pH of 7.0 or pH 7.5 (see Example 4 at columns 11-12). The pH levels disclosed by Beckert, such as pH of 7.0 or pH 7.5 read on the pH levels of the small and large intestines (pH of small intestine is known to be generally 7-8 and pH of large intestine is generally in the range of 5.5-7). Furthermore, the Beckert reference explicitly teaches that the "release characteristics are advantageous for some active ingredient substances which are intended to be released in the intestine". See column 2, lines 39-50. Thus, the reference clearly desires release of active agent in the intestines and would include both the small and large intestines. Hence, Appellant's arguments were not held persuasive.

(11) Related Proceeding(s) Appendix

No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

/Humera N. Sheikh/

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